UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,088	12/27/2005	Richard James Lewis	16096	9222

272 7590 10/10/2007

SCULLY, SCOTT, MURPHY & PRESSER, P.C.
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
10/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,088	LEWIS ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,12,13,23,27,28,38-41,43,45,47 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-4, 7-11, 14-22, 24-26, 29-37, 42, 44, 46, 48 and 50-52 in full and 1, 5, 6, 12, 13, 23, 27, 28, 38-41, 43, 45, 47 and 49 in part.

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group 208, claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49, to the extent that these claims read on SEQ ID NO:5 or SEQ ID NO:3 in which Xaa5 and Xaa6 are both present and are any amino acid but C, in the reply filed on September 4, 2007 is acknowledged. As discussed in the previous Office action, Xaa1 is pyroglutamate, Xaa2 is absent, Xaa3 is G and Xaa4 is V. Thus, the elected sequences are EGVCCGYKLCXXC in which X is not C (the extent to which SEQ ID NO:5 reads on the elected sequence) and CCGYKLCXXC in which X is not C (the extent to which SEQ ID NO:3 reads on the elected sequence). Claims 2-4, 7-11, 14-22, 24-26, 29-37, 42, 44, 46, 48 and 50-52, as well as claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49 to the extent that they do not read on the elected sequences, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. No claims have been amended, canceled or added. Accordingly, claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49 to the extent that they read on the elected invention are examined on the merits herewith.

In their traversal, Applicants assert that all of their many inventions are related to a single general inventive concept, which is that a certain part of a χ-conotoxin is essential for biological activity and that χ-conotoxin activity may be enhanced by modifying the conotoxin at certain positions. Applicants note that their claims should be considered as a whole. In reply, the claims have been considered as a whole. Applicants have not stated which portions of which polypeptides can be modified to enhance their activity, which amino acid positions should be modified or what these modifications are. As previously discussed, the necessary criterion

for unity of invention is that a technical feature that is shared by all of the groups of claims be special, i.e., novel and not obvious. That the different inventions are related to a general concept does not provide for unity of invention. As previously discussed, each polypeptide is a different structure, requiring a different search, and, as a result, a common technical feature is not present. Because a common technical feature is not present, a special common technical feature is not present.

In view of the foregoing, the restriction requirement is deemed proper and is made final.

Claim Objections

Claims 1, 27 and 28 are objected to because of the following informalities. The claims recite that the conotoxin polypeptide has the ability to inhibit neuronal amine/noradrenaline transporter, rather than "a neuronal amine transporter" or "a neuronal noradrenaline transporter." Appropriate correction is required, as the claims must be written in standard English to comply with U.S. patent practice.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite an

infinite genus of variants of SEQ ID NOS: 3 and 5 in which G, Y, K and/or L are replaced by any "conservative" amino acid substitution. The term "conservative amino acid substitution" is not defined in the specification, and only one or two examples are provided for each of these amino acids in isolation. No species of this genus are disclosed, i.e., no polypeptides that are conservatively substituted variants of SEQ ID NOS: 3 or 5, with or without conserved function. Therefore, one skilled in the art would have no idea which species of the claimed genus Applicants intended to include within the scope of the invention, and one skilled in the art cannot reasonably conclude that Applicants had possession of the claimed invention at the time the instant application was filed.

Consequently, there is no evidence that a sufficient number of representative species of this vast genus were in the possession of the inventors at the time of filing. To satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. Because no species of the claimed genus are disclosed, the claims fail to satisfy the written description requirement.

Claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:3 or 5, does not reasonably provide enablement for a polypeptide that is a variant of SEQ ID NO:3 or 5 having conservative amino acid substitutions for G, Y, K and/or L. As a result, the specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether or not undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue

experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

The claims are very broad because they recite any variant of SEQ ID NO:3 or 5 having unlimited "conservative" substitutions at the amino acid positions of the G, Y, K and L residues.

2. The nature of the invention.

The invention is designed to provide novel conotoxins that are SEQ ID NO:3, 5 or variants thereof.

3. The state of prior art.

See the discussion of McIntosh et al. (US 6,767,896 B1) and Olivera et al. (US 2003/0109670 A1) below.

4. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Because the effect of making changes to the claimed polypeptide sequences (SEQ ID NOS:3 and 5) at the G, Y, K and L positions is not known or disclosed in the specification, particularly the effect on the conotoxin activity (analgesic and anti-inflammatory activity), the

specification needs to have more detail so that the properties of variants of SEQ ID NO:3 and 5 will be predictable. Because the prior art and the instant specification do not disclose any conservatively substituted variants of SEQ ID NO:3 or 5 having the same conotoxin activities, it cannot be predicted that any such variants would retain the activities of SEQ ID NO:3 or 5.

6. The amount of guidance present.

As noted above, Applicants have not provided any specific guidance for preparing any conservatively substituted variants of SEQ ID NO:3 or 5. The general guidance on p. 11 of the specification, that any G anywhere in any polypeptide may be replaced with A, or that any L anywhere in any polypeptide may be replaced with I, is not specific guidance. The claims are not limited to G-to-A or L-to-I substitutions, as what may be substituted is unlimited in type and number, and no variants have been made.

7. The existence of working examples.

The specification contains no working examples disclosing any conservatively substituted variants of SEQ ID NO:3 or 5.

8. The quantity of experimentation necessary.

To prove that any conservatively substituted variant of SEQ ID NO:3 or 5, varied at the G, Y, K and L amino acid positions, would retain the conotoxin properties of SEQ ID NO:3 or 5, many experiments would have to be conducted under a wide range of conditions. In these experiments, many sets of variant polypeptides would have to be made, each set having a different number and permutation of amino acids substituted, e.g., G only, G and Y, G and K, Y and L, G, Y and L, etc. For each set, many subsets would have to be prepared, each subset having a different group of amino acids used as substituents. Many different groups would have to prepared and tested for each subset, the groups varying significantly in their composition, as "conservative" substitutions are not a defined term in the specification. A conotoxin activity that

is the same as that of SEQ ID NO:3 or 5 would have to be identified for each variant in each group in each subset, requiring an infinite amount of random testing in a wide variety of assays for the reduction of pain and inflammation.

These types of experiments and data are missing from the specification. A great deal of experimentation is needed to establish that any conservatively substituted variant of SEQ ID NO:3 or 5 has the conotoxin activity of SEQ ID NO:3 or 5, because these polypeptides are claimed, and no disclosure of such polypeptides is provided. Even if one such variant polypeptide could be made and identified, by random, trial-and-error construction and testing, without a very large amount of data, such a result could not be expected with a different polypeptide, particularly when tested in a different assay, or under different assay conditions, than the first variant.

In view of the foregoing, the claims fail to satisfy the enablement requirement.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by McIntosh et al. (US 6,767,896 B1). McIntosh et al. disclose compositions comprising the conotoxin polypeptides Mar1 (SEQ ID NO:12) and Q818 (SEQ ID NO:14), which comprise the sequence of Applicants' SEQ ID NO:3- CCGYKLCXXC (see col. 6, lines 57-62; col. 10, line 66,

to col. 15, line 54; col. 20, Table 1; and col. 22, Table 2). These conotoxins are paralytics that inhibit neurotransmitter activity but that do not have an anticholinergic effect (they are not α-conotoxins) (see col. 1, line 26, to col. 2, line 13). McIntosh et al. do not disclose the mechanism of action by which these conotoxins work, i.e., that they are inhibitors of a noradrenaline transporter. But, reciting the mechanism of action of the claimed polypeptide does not make the composition patentable, as the mechanism of action is an inherent feature of the molecules that participate in that particular mechanism. What inherently occurs for a particular molecule has no patentable weight. McIntosh et al. disclose the claimed compositions.

In view of the foregoing, a holding of anticipation is required.

Claims 1, 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Olivera et al. (US 2003/0109670 A1). Olivera et al. disclose a composition comprising the conotoxin polypeptide Mr1.1 (SEQ ID NO:351), which comprises the sequence of Applicants' SEQ ID NO:3- CCGYKLCXXC (see p. 41, Table 5; and paragraphs 3, 5, 6, 9, 11, 23, 24 and 48-56). The conotoxin is a paralytic that inhibits neurotransmitter activity but that does not have an anticholinergic effect (it is not an α-conotoxin) (see paragraphs 5-6). Olivera et al. do not disclose the mechanism of action by which the conotoxin works, i.e., that it inhibits a noradrenaline transporter. But, reciting the mechanism of action of the claimed polypeptide does not make the composition patentable, as the mechanism of action is an inherent feature of the molecules that participate in that particular mechanism. What inherently occurs for a particular molecule has no patentable weight. Olivera et al. disclose the claimed composition.

In view of the foregoing, a holding of anticipation is required.

Double Patenting- Obviousness-type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 6, 12-13, 23, 27, 28, 38-41, 43, 45, 47 and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 10/537,704. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims is drawn to a composition comprising the same polypeptide, instantly claimed SEQ ID NO:5. Each set of claims recites the same invention with slightly different wording that amounts to a semantic equivalent. Thus, the two inventions are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652

rk/2007-09-26

Rosanne Kosson

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1600~~ 1600

51. (New) The peptide according to claim 2, wherein the Tyr of loop 1 has been replaced with MeY and/or the Leu of loop 1 is replaced with Hle or Nle.

52. (New) The peptide according to claim 7, wherein the Tyr of loop 1 has been replaced with MeY and/or the Leu of loop 1 is replaced with Hle or Nle.